REMARKS

Claim 61 is pending in the subject application. By this Amendment, applicants have amended claim 61. Support for the amendments to claim 61 may be found in the specification *inter alia* on page 27, at lines 4-21. Applicants maintain that the amendments to claim 61 raise no issue of new matter. Accordingly, applicants respectfully request that the Examiner enter this Amendment. Upon entry of this Amendment, claim 61, as amended, will be pending and under examination.

Rejection under 35 U.S.C. §112, Second Paragraph

On page 1 of the October 17, 2007 Final Office Action, the Examiner indicated that the previous rejection of claim 61 on the ground of indefiniteness had been withdrawn.

37 C.F.R. §1.98

On page 1 of the October 17, 2006 Office Action, the Examiner states that in an initial review of ten U.S. patents and published applications listed on the PTO-Form 1449 submitted with an Information Disclosure Statement filed August 2, 2006, only one of these documents was found to be material to patentability of the claim in accordance with 37 C.F.R. §1.56. The Examiner then stated that in view of the low percentage of references material to patentability in the sampled documents, the August 7, 2006 Information Disclosure Statement is not in compliance with 37 C.F.R. §1.56 and §1.98 and the remaining references listed on the PTO-Form 1449 will not be considered.

According to 37 C.F.R. §1.97(c), "An information disclosure statement shall be considered by the Office if filed after the period specified in paragraph (b) of this section, provided that the information disclosure statement is filed before the mailing date of any of a final action under § 1.113, a notice of allowance under § 1.311, or an action that otherwise closes prosecution in the application, and it is accompanied by one of: (1) The statement specified in paragraph (e) of this section; or (2) The fee set forth in § 1.17(p)." (Emphasis Added). The Information Disclosure Statement in question was filed in

accordance within the time period specified in 37 C.F.R. §1.97(c) and in all other respects complies with the requirements of 37 C.F.R. §1.97(c).

37 C.F.R. §1.97(i) states that the only basis for not considering an information disclosure statement is its failure to comply with 37 C.F.R. §1.97 or §1.98.

In refusing to consider applicants' information disclosure statement, the Examiner has stated that it is not in compliance with 37 C.F.R. §1.56 and §1.98.

There is nothing in 37 C.F.R. §1.56 which is a basis for refusing to consider an information disclosure statement, and as noted above, 37 C.F.R. §1.97 specifically states the only basis for the Office not complying with the mandatory "shall be considered" language of 37 C.F.R. §1.97(c) is applicants' failure to comply with 37 C.F.R. §1.97 or §1.98. Thus, the Examiner's reference to 37 C.F.R. §1.56 as a justification for refusing to consider applicants' information disclosure statement is misplaced. In fact, 37 C.F.R. §1.97(h) specifically states that "The filing of an information disclosure statement shall not be construed to be an admission that the information cited in the statement is, or is considered to be, material to patentability as defined in § 1.56(b)."

37 C.F.R. §1.98 only sets forth requirements as to the content of the information disclosure statement itself, not the content of the references cited therein. Thus, there is also nothing in §1.98 which justifies the Examiner's refusal to consider applicants' information disclosure statement.

Accordingly, applicants maintain that the Examiner is required to review their Information Disclosure Statement which complies with requirements of 37 C.F.R. §1.98 and 37 C.F.R. §1.97. The fact that the Examiner considered only one of the ten documents he reviewed material to the patentability of the claim is not a proper basis for the Examiner to refuse to consider the remaining references. The Information Disclosure Statement in question clearly complies with 37

C.F.R. §1.97 and §1.98 and therefore the references should be considered. Applicants again request that the Examiner consider the references listed in the August 7, 2006 Information Disclosure Statement, initial the PTO-Form 1449 submitted therewith, and return a copy of the initialed PTO-Form 1449 to applicants. For the Examiner's convenience, applicants attach hereto as **Exhibit A**, a copy of the August 2, 2006 PTO-Form 1449, which is hereby resubmitted.

Rejection under 35 U.S.C. §112, First Paragraph

The Examiner stated that claim 61 stands rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Specifically, the Examiner alleged that the original application does not provide adequate support for the broadly claimed genus of agents. The Examiner stated that claim 61 does not limit the genus to any particular type of compound or any particular family of compounds. Thus, the Examiner stated that the genus corresponding to the agent encompasses an inordinate number of unrelated species.

In response, applicants respectfully traverse the Examiner's rejection. Nevertheless, without conceding the correctness of the Examiner's ground of rejection, applicants have amended claim 61 to recite "a chemokine antagonist" rather than an agent.

Applicants' Invention As Recited In Amended Claim 61

Applicants' invention as recited in amended claim 61 provides a method of inhibiting infection of a CD4+ cell by a macrophage-tropic HIV-1 which comprises contacting the CD4+ cell with a chemokine antagonist which (a) binds to a CCR5 chemokine receptor on the surface of the CD4+ cell; (b) blocks fusion of HIV-1_{JR-FL} with a PM-1 cell; (c) does not block fusion of HIV-1_{BRU} with such PM-1 cell; and (d) does not

activate an inflammatory response upon binding to the CCR5 chemokine receptor on the surface of the CD4+ cell; in an amount and under conditions such that fusion of the macrophage-tropic HIV-1 to the CD4+ cell is inhibited, so as to thereby inhibit infection of the CD4+ cell by the macrophage-tropic HIV-1.

According to the Examiner, the factors to be considered in determining whether there is sufficient evidence of possession of an invention by an applicant include: (1) the level of skill and knowledge in the art, (2) physical and/or chemical properties of the claimed genus, (3) functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and (4) the method of making or using the claimed invention.

The Level Of Skill And Knowledge In The Art

Applicants maintain that the level of skill in the art as of the effective filing date was high in the field of biotechnology. One skilled in the art can use applicants' disclosure together with general knowledge in the field to readily understand and envisage applicants' invention as recited in amended claim 61. According to the Guidelines For Examination Of Patent Applications Under The 35 U.S.C. 112, ¶1, "Written Description" Requirement, Federal Register Vol. 66, No. 4, p. 1105, Section IIA(2) states that "[g]enerally, there is an inverse correlation between the level of skill and knowledge in the art and the specificity of disclosure necessary to satisfy the written description requirement." Accordingly, applicants maintain that the requirements for the disclosure to satisfy the written description requirement where the level of skill in the relevant art is high is less than it would be if the level of skill in the art were low. Thus, one skilled in the art does not require a more specific disclosure than applicants' disclosure. In addition, applicants note that on page 9 of the February 3, 2006 Office Action previously issued in connection with the subject application, the Examiner acknowledged that the level of skill in the biotechnology art was high at the time of filing.

Physical And/Or Chemical Properties Of The Claimed Genus

The claimed genus recited in amended claim 61 encompasses compounds which are chemokine antagonists which bind specifically to the CCR5 chemokine receptor. Applicants maintain that one skilled in the art would readily understand a chemokine antagonist to be a compound which, upon binding to a chemokine receptor, inhibits the receptor-mediated response activated by the binding to the receptor of its endogenous ligand(s). As disclosed in the application, and as recited in amended claim 61, the chemokine antagonist binds to a CCR5 chemokine receptor on the surface of a CD4+ cell and does not activate an inflammatory response upon binding to the CCR5 chemokine receptor on the surface of the CD4+ cell. Applicants maintain that the binding specificity of the chemokine antagonist to the CCR5 chemokine receptor provides sufficient disclosure for one skilled in the art to understand the scope of the now claimed genus of "chemokine antagonist".

Moreover, the chemokine antagonist recited in amended claim 61 binds to the known CCR5 chemokine receptor for which endogenous chemokine ligands are known in the art in addition to those disclosed in the specification. Specifically, chemokines are disclosed *inter alia* in the specification at page 1, line 32 to page 2, line 3; page 2, lines 28-34; page 7, lines 3-30; Figure 1; page 26, lines 8-18; page 34, lines 33-37; and page 35, Table 2a.

In addition, multiple examples of chemokine antagonists are disclosed in the subject application, e.g. derivatives of chemokines, such as N-terminal derivatives of RANTES including Met-RANTES, and antibodies to the CCR5 chemokine receptor. These are the very compounds which the Examiner has acknowledged are adequately described. (See the October 17, 2006 Final Office Action on page 5 beginning in the middle of the page with "It is noted that ...") Moreover, the Examiner has apparently failed to note or acknowledge the disclosure beginning on page 26, line 29 and continuing to page 28, line 25, of chemokine derivatives that inhibit HIV-1 fusion, including N-terminal derivatives of RANTES, MIP1-α, MIP1-β, such as Met-RANTES, and N-

peptide having a deletion of 8 amino acids at the N-terminus of MCP-1. The specification also discloses at page 12, CCR5-specific monoclonal antibodies, namely, 2D7, PA8, PA9, PA10, PA11, and PA12, which are also chemokines antagonists that inhibit infection of CD4+ cells by HIV-1.

Applicants maintain that the knowledge in the art and the disclosure of the subject specification provide a more than adequate written description of the common physical and chemical properties of chemokine antagonists, so that one skilled in the art could readily envisage the now claimed genus of chemokine antagonists.

Known Or Disclosed Correlation Between Structure And Function

As stated above, the physical and chemical characteristics of the claimed chemokine antagonists would be readily recognizable by one skilled in the art in light of the disclosure of the subject application and the knowledge in the art at the time of filing the subject application. In addition, applicants maintain that the functional properties of the chemokine antagonists are fully disclosed in the specification and recited in amended claim 61, i.e. blocking fusion of a PM-1 target cell with HIV-1_{JR-FL} but not blocking fusion of such PM-1 target cell with HIV-1_{BRU}, and binding to the CCR5 chemokine receptor, but not activating an inflammatory response upon binding to the CCR5 chemokine receptor on the surface of the CD4+ cell.

Applicants maintain that the specification discloses the relationship between the physical/chemical properties and the function of the claimed chemokine antagonists. As explained starting on page 36, line 17, CCR5 (also known as C-C CKR-5) is the co-receptor with CD4 needed for HIV-1 entry into a cell. At page 36, lines 20-22, the specification states that "[i]t has been known for a decade that HIV-1 requires a second receptor for entry into CD4+ cells". As stated on page 36, lines 35-37, and as shown on page 37, Table 3, "[t]he expression of C-C CKR-5 on Hela-CD4 (human), COS-CD4 (simian) and 3T3-CD4 (murine) cells rendered each of them readily infectible by the primary, NSI strains ADA and BaL in the env-complementation assay of

HIV-1 entry." Accordingly, applicants maintain that the specification discloses that HIV-1 requires two receptors for entry into a CD4+ cell, the second receptor being CCR5, and that the blocking of HIV-1 gp120 binding to CCR5 would inhibit entry of HIV-1 into a CD4+ cell. Thus, applicants maintain that one skilled in the art would understand the physical and chemical properties of the chemokine antagonists which enable them to bind to the CCR5 chemokine receptor on the surface of a CD4+ cell, and to block fusion of a CD4+ cell with a macrophage-tropic HIV-1, but not with a T-cell tropic HIV-1. Accordingly, applicants maintain that the specification clearly describes the correlation between the identifying properties and the function of the chemokine antagonists recited in amended claim 61.

Method Of Using The Claimed Invention

Applicants also maintain that the specification discloses a method, i.e. the RET assay, for readily identifying additional chemokine antagonists having the properties as recited in claim 61. Applicants respectfully disagree with the Examiner's assertion that this assay is insufficient to show that applicants had possession of the claimed invention at the time of filing. Applicants maintain as an initial matter that independent of the RET assay the subject application provides an adequate written description of chemokine antagonists. Moreover, the RET assay specifically identifies chemokine antagonists with the properties recited in amended claim 61. Applicants maintain that the RET assay disclosed is not merely a generic methodology. Based on applicants' disclosure, one skilled in the art can readily perform the disclosed RET screening assay to identify chemokine antagonists as recited in claim 61. Applicants note that one skilled in the art is also provided with working examples in which this assay was used to identify chemokine antagonists with the claimed properties (see, for example, pages 35-36, Table 2a and Table legend). Accordingly, applicants maintain that the instant specification provides a written description of chemokine antagonists that is adequate to establish applicants' possession of the now claimed invention.

In addition, applicants note that the specification discloses at page 15, lines 12-24, a second method for identifying chemokine antagonists as recited in amended claim 61. Specifically, the specification discloses the following assay as a method of identifying chemokine antagonists: 1) incubating soluble CD4 with biotinylated gp120 from HIV-1_{JR-FL}; 2) incubating this complex with CCR5-expressing cells that do not express CD4 in the presence of absence of a candidate chemokines antagonist; 3) washing and incubating with streptavidin-phycoerythrin; and 4) washing and measuring the amount of bound gp120 using a flow cytometer or fluorometer and calculating the degree of inhibition of binding by the candidate chemokines antagonist.

Accordingly, applicants maintain that the application discloses and describes numerous chemokine antagonists, as well as methods of identifying more chemokine antagonists, and further establishes applicants' possession of the invention as now claimed.

In view of the foregoing remarks, applicants maintain that the specification satisfies the written description requirement of 35 U.S.C. §112, first paragraph, with regard to claim 61 as amended herein, and request that the Examiner reconsider and withdraw this ground of rejection.

Conclusion

Applicants maintain that in view of the remarks set forth above, the ground of the Examiner's rejection has been overcome. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection of claim 61, and request allowance of this pending claim as amended.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.